PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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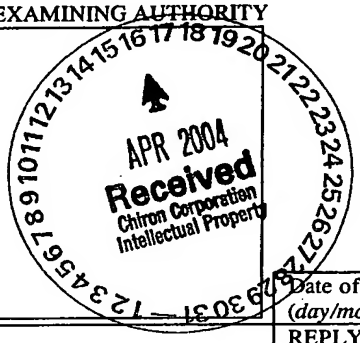

PCT

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference 19016.002	Date of Mailing *(day/month/year)* 12 APR 2004 REPLY DUE within 1 months/days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US03/06742	03 March 2003 (03.03.2003)	01 March 2002 (01.03.2002)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 38/16 and US Cl.: 514/12

Applicant

CHIRON CORPORATION

1. This written opinion is the first (first, etc,) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 03 July 2003(03.07.2003).

Name and mailing address of the IPEA/US
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Form PCT/IPEA/408 (cover sheet)(July 1998)

4/16/04 WMS
CJS
P81P19016.002
5/12/04-RSD
to finish Written Opinion

WRIT[redacted]OPINION

International application No.
PCT/US03/0[redacted]

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☒ the description:
pages 1-49, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 50-56, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-2, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE _____

☐ the claims, Nos. NONE _____

☐ the drawings, sheets/~~fig~~ NONE _____

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*

WRITTEN OPINION

International [redacted]ation No.
PCT/US03/06[redacted]

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims NONE	YES
	Claims 1-56	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-56	NO
Industrial Applicability (IA)	Claims 1-56	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-4, 11, 17, 36, 48-50 and 54 lack novelty under PCT Article 33(2) as being anticipated by Sanofi-Synthelabo. Sanofi-Synthelabo teaches administration of GSK3 inhibitors to treat cerebrovascular accidents(see abstract). It further teaches that the GSK3 inhibitors may be supplemented with an active ingredient of another medicament for the treatment of the above mentioned diseases (cerebrovascular accident). Adminstration of the GSK3 inhibitors is *inter alia* intracerebrally and orally(page 6, line 58 to page 7, line 31).

Claims 1, 17, 36, 48-50 and 54 lack novelty under PCT Article 33(2) as being anticipated by Eldar-Finkelman. The prior art teaches GSK-3 inhibitors to be useful of treatment of biological conditions mediated by GSK-3 activity such as treatment of conditions of ischemic insult such as cerebral stroke to prevent, halt or reduce neuronal cell death (page 4, paragraph 0042). Formulations are administered parenterally as well as enterally (page 8, paragraph 0081). Co-administraton of another agent known to treat the biological condition is disclosed on page 7, paragraph 0069.

Claims 1, 17, 36, 48-50 and 54 lack novelty under PCT Article 33(2) as being anticipated by Sanofi-Synthelabo. Sanofi_Synthelabo teaches administration of GSK3 inhibitors to treat cerebrovascular accidents(page 2, lines 10-19). It further teaches that the GSK3 inhibitors may be supplemented with an active ingredient of another medicament for the treatment of the above mentioned diseases (cerebrovascular accident). Adminstration of the GSK3 inhibitors is *inter alia* intracerebrally and orally(page 20, line 33 to page 21, line 33).

Claims 1-56 lack novelty under PCT Article 33(2) as being anticipated by Nuss et al. Nuss et al. teach GSK 3 inhibitors to treat *inter alia* brain injury (see abstract) such as cerebral ischemia (page 1, paragraph 0001). The GSK3 inhibitors can be administered with other therapeutically active agents known to treat cerebral ischemia. The compounds can be administered enterally and parenterally (page 12, paragraph 0102).

WRITTEN OPINION

International Application No.
PCT/US03/[illegible]742

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:
The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.